REMARKS

Claims 1-7 and 11 presently appear in this case. No claims have been allowed. The official action of October 23, 2002, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to DNA encoding the human MORT-1 protein and fragments and analogs thereof, as well as vectors, transformed host cells and methods of producing same. The invention also relates to a recombinant animal virus vector which includes such a sequence, as well as a virus surface protein capable of binding a specific target cell surface receptor.

The examiner states that the priority date of the present application is October 14, 1995, as applicants' three foreign priority applications are not available in certified and translated copies. The examiner states that applicants have been invited to submit evidence pointing to the serial number, page and line where support can be found establishing an earlier priority date.

filing date 10/2-

The examiner's attention is respectfully invited to parent application 08/860,082. In the official action dated November 10, 1998, the examiner acknowledged applicants' claim for priority and receipt of all of the certified copies of the priority documents. As the priority documents are in the

English language, it is not necessary to submit any translations. For the examiner's convenience, attached hereto are non-certified photocopies of the previously-filed priority documents. In order to overcome the art rejections of record, it is at least necessary to establish that applicants are entitled to the priority date of Israel application 112692, filed February 19, 1995. Note that the sequence of the present SEQ ID NO:2 is the deduced amino acid sequence in Figure 8. Note claims 16-19 as originally filed, as well as claim 3, from which they ultimately depend. This claim includes DNA sequences capable of hybridization to the sequence of HF1 (MORT-1) under moderately stringent conditions. Vectors containing such DNA, as well as host cells and methods for producing the proteins by means of the host cells are disclosed in the last paragraph of page 10. As to the recombinant animal virus vector, which includes the sequences of the HF1 protein, see page 16, in the sub-paragraph beginning at line 6. Note also particularly the penultimate paragraph on page 16 and the first paragraph on page 17. For active fragments, see the first line of page 29 of the priority document. Accordingly, it is urged that all of the present claims are supported by the disclosure of the English-language certified priority document of Israeli application 112692, filed February 19, 1995, which is of

record in the parent application as acknowledged by the examiner in the official action of November 10, 1998. Accordingly, it is requested that the examiner acknowledge that applicants are entitled to a priority date at least as early as February 19, 1995.

Claims 1-7 and 11 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for the use of the language "moderately stringent conditions". The examiner states that moderately stringent conditions are not defined by the claim, and the specification does not provide a standard for ascertaining the requisite degree of moderately stringent conditions and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention and would not be able to determine metes and bounds of the claims. This rejection is respectfully traversed.

The language "under moderately stringent conditions" is not unduly vague and indefinite. MPEP §2173.02 states:

> The examiner's focus during examination of claims for compliance with the requirement for definiteness of 35 U.S.C. §112, second paragraph is whether the claim meets the threshold requirements of clarity and precision, not whether more suitable language or modes of expression are available. ...
>
> The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim

> language must be analyzed, not in a vacuum, but in light of:
>
> (A) the content of the particular application disclosure;
>
> (B) the teachings of the prior art; and
>
> (C) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

At the time the present invention was made, the metes and bounds of moderate stringency were known to those of skill in the art, even though there may be some variation in the means for providing roughly the same level of stringency either at the hybridization stage or at the wash stage. U.S. patent 5,026,636, relevant pages of which are attached, was available at the time the invention was made and defines moderate stringency as conditions that allow detection of nucleotide sequences at least approximately 75% homologous to the probe (column 4, lines 50-65). This patent further teaches that moderately stringent conditions for a particular probe, when seeking a specified degree of homology, may be readily determined by those of skill in the art using, for example, the reference text, Nucleic Acid Hybridisation: A Practical Approach, Hames and Higgins, eds., IRL Press, Washington (1985) or the scientific publication, Wood et al, Proc Natl Acad Sci USA 82:1585-1588 (1985) (copy of which is attached hereto), for guidance. Chapter 4 of Nucleic Acid

Hybridisation: A Practical Approach, on quantitative filter hybridization, a copy of which is attached hereto, teaches the various factors affecting hybrid stability through a calculation of melting temperature (T_m) of the hybrid using the standard equation (Equation 7 on page 80) and factoring in the percent mismatch (percent identity) that is sought. The calculation of T_m takes into account the molarity of the monovalent cation (i.e., sodium in SSC solution). Accordingly, those of skill in the art would recognize and understand what the metes and bounds of the conditions needed for moderate stringency hybridization to detect a hybrid with a specified percent identity, e.g., 75%.

Indeed, U.S. patents 4,968,607 (50°C, 2 X SSC; column 10, lines 39-40), 5,171,675 (50°C, 2 X SSC; column 6, line 49), 5,198,342 (50°C, 2 X SSC; column 9, lines 54-55), 5,262,522 (50°C, 2 X SSC; column 15, lines 8-9), and 5,237,051 (60°C, 1 X SSC; column 5, lines 24-27), which were available to the art at the time of the present invention, demonstrate that those in the art were able to determine and define moderately stringent conditions based on the knowledge and skill at that time. All have claims which include the term "moderate stringency". Relevant pages of the above-cited U.S. Patents are attached hereto. According to the Federal Circuit Court of Appeals, it is relevant to the issue of definiteness

that the criticized words are used frequently in patent claims. See *Andrew Corp. v. Gabriel Electronics*, 6 USPQ2d 2010, 2012-13 (Fed. Cir. 1988). And see also *Ex parte Brian*, 118 USPQ 242, 245 (POBA 1958), where it states:

> Since the claims under consideration are similar to those in the patents, we do not feel disposed to reject them and thus upset such a long established practice in the particular art under consideration.

In other words, the very fact that "moderate stringency" claims have been repeatedly allowed in the past is reason to consider them definite. This is true, not only because the use of such claims by many different inventors and allowed by many different examiners is evidence that the terminology is considered sufficiently definite by the art, but also because a reinterpretation of the definiteness of such claims by the PTO casts a shadow of doubt on previously issued "moderate stringency" claims, even though such claims are entitled to a presumption of validity.

Furthermore, the widely used reference text, Current Protocols in Molecular Biology, eds. Ausubel et al, John Wiley & Sons, Inc., (1987-1998) on page 2.10.11 (Supplement 26, 1994[1]), a copy of which is also attached, guides those of skill in the art how to use a rational approach at determining

---

[1] A copy of page 2.6.1 is also attached which shows that Supplement 26 is dated 1994).

"moderate stringency" wash conditions by calculating the decrease in temperature required using the correlation for decrease in T_m per percent mismatch.

Accordingly, in view of the teachings of the prior art, it is urged that the claim interpretation to be given to the term "hybridization under moderately stringent conditions" are those conditions which would permit detection of nucleotide sequences at least approximately 75% homologous. Thus, the scope of the invention sought to be patented can be determined from the language of the claims with a reasonable degree of certainty. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

The examiner states that claim 11 is indefinite because claim 11 is dependent on non-elected claim 8.

OK

Claim 11 has now been amended so as to depend from claim 1, thus obviating this part of the rejection.

written description rejection

Claim 1, item 2, and claims 2-7 and 11 have been rejected under 35 U.S.C. §112, first paragraph, in view of their recitation of a DNA sequence that encodes an analog of MORT-1 that binds with FAS-IC and that is capable of hybridizing to the cDNA encoding SEQ ID NO:2 under moderately stringent conditions. The examiner states that it is not clear whether cell death is due to the activation of FAS ligand receptor by MORT-1 protein or due to the expression of

p55-IC in the transfected cells. The examiner states that binding to the FAS ligand receptor is only a physical property and not a function of the MORT-1 protein encoded by the claimed polynucleotide because it has not been shown that the binding alone by MORT-1 protein to the FAS ligand receptor is sufficient for the activation of FAS ligand receptor. The examiner further states that the instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of sub-genera, including full-length genes. The examiner states that, since the disclosure fails to describe the common attributes or characteristics that identify members of the genus and because the genus is highly variant, the disclosure of the specific nucleotide sequences and the ability to screen is insufficient to describe the genus. This rejection is respectfully traversed.

First, the examiner's comments about whether or not the function of binding to FAS-IC is merely a physical property or is required for cell death is irrelevant. The claims only require the property of binding to FAS-IC, and this property is sufficient to establish utility for the protein. If it binds to FAS-IC, it can be used to isolate FAS-IC by affinity chromatography. Thus, this physical property is sufficient to establish utility for the DNA of the

present invention, and it is irrelevant whether or not the examiner considers that the additional properties of cell death or activation of FAS ligand receptor are adequately established.

As to the question of whether or not the full scope of presently claimed analogs is supported by sufficient written description in view of the fact that only a single species is disclosed in the specification, reference is made to Example 14 of the Revised Interim Written Description Guidelines training materials. In that example, a claim directed to a specific protein and variants thereof that are at least 95% identical thereto and have the same function was considered to be adequately supported by written description only of a single species. The analysis indicated that procedures for making variants of the specific species were conventional in the art, and an assay was described which would identify other proteins having the claimed catalytic activity. The same certainly is true here. The training materials state that the procedures for making variants that have 95% identity to the specified species and retain its activity are also conventional in the art. Here, the procedure for determining variants by hybridization of moderate stringency is conventional in the art. In the training materials, it was recognized that the claim has two

different generic embodiments, the first being a protein which comprises the specified sequence, and the second being variants of the specified sequence. As here, there was only a single species disclosed, and the examiner has conceded that the specified species is novel and unobvious. The training materials then conclude that the single species disclosed is representative of both generic embodiments because all members have at least the specified amount of structural identity with the reference compound and because of the presence of an assay that applicant provided for identifying all of the compounds having the specified amount of structural identity that are capable of the specified activity, in this case binding to FAS-IC. Thus, the training materials conclude that one of skill in the art would have concluded that applicant was in possession of the necessary common attributes possessed by the members of the species.

It is urged that the same analysis establishes that applicant was in possession of the necessary common attributes possessed by members of the genus of those analogs that are encoded by DNA which bind DNA which encodes SEQ ID NO:2 under conditions of moderate stringency and which retain the ability to bind to FAS-IC. Therefore, as the single species is representative of the genus, the disclosure must meet the requirement of 35 U.S.C. §112, first paragraph, as providing

adequate written description for the claimed invention. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

OK withdrawn

Claim 11 has been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in that it is drawn to a pharmaceutical composition for modulating the FAS-R ligand effect on cells and *in vivo* use is inherent in a pharmaceutical composition. This rejection is respectfully traversed.

Claim 11 has now been amended to change it from a composition claim to a claim directed only to the recombinant animal virus vector. No inherent *in vivo* use is present in claim 11. Accordingly, as amended, this rejection is no longer applicable. Reconsideration and withdrawal thereof are, therefore, respectfully urged.

OK withdrawn

Claim 11 has been rejected under 35 U.S.C. §112, first paragraph, for lack of enablement on the ground that the specification does not reasonably provide enablement for a recombinant animal virus vector encoding a protein capable of binding any cell surface receptor and MORT-1 protein of SEQ ID NO:2. This rejection is respectfully traversed.

Claim 11 has now been amended to specify that the recombinant animal virus vector encodes a virus surface

protein capable of binding a specific target cell surface receptor. In this regard, reference is made to the present specification at the first paragraph on page 30. It is urged that in view of this revised language, the present rejection has now been obviated. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

withdrawn Claims 1(1) and (3) have been rejected under 35 U.S.C. §102(a) as being anticipated by Boldin et al in the Genbank Sequence Database made publicly available on April 1995. This rejection is respectfully traversed.

First of all, Boldin et al is a publication of the present inventors. Secondly, as indicated above, applicants are entitled to an effective filing date at least as early as February 19, 1995. Accordingly, the Boldin Genbank Sequence Database is not available as a reference. Reconsideration and withdrawal of this rejection are respectfully urged.

withdrawn Claims 1(2) and (3) and 2 have been rejected under 35 U.S.C. §102(a) as being anticipated by Chinnaiyan in the Genbank Database made publicly available in 1995 and Cell 81:505-512 (1995). This rejection is respectfully traversed.

Attached hereto is the revision history of Accession Nos. U24231 and Q13158. It can be seen that the earliest date of public availability of either was May 20, 1995. Furthermore, the Cell publication was published on May 19,

1995, as can be seen from the attached copy of the PubMed Abstract. As it has been shown hereinabove that the present application is entitled to a priority date of at least as early as February 19, 1995, reconsideration and withdrawal of this rejection are in order.

Claim 1, items 1, 2 and 3, and claims 2-7 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Boldin and Chinnaiyan in view of USP 4,889,806 and Sanbrook 1989. This rejection is respectfully traversed.

As neither of the two primary references are available as references in view of their date for the reasons discussed hereinabove, the present rejection must fall. Reconsideration and withdrawal of this rejection are, therefore, also respectfully urged.

It is submitted that all of the claims now present in the case clearly define over the references of record and fully comply with 35 U.S.C. §112. Reconsideration and allowance are, therefore, earnestly solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By
Roger L. Browdy
Registration No. 25,618

RLB:rd
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
G:\BN\I\inl2\Wallach16A\Pto\AmendmentC.doc